

# HIV Treatment as Prevention and “The Swiss Statement”: in for a Dime, in for a Dollar?

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(See the article by Hasse et al, on pages 1314–1322.)

For more than 20 years, investigators have been working to develop a well-tolerated, reliable combination of antiviral agents that render the human immunodeficiency virus (HIV)-infected patient who is receiving therapy less contagious [1]. This goal gained support from remarkable advances in the prevention of vertical transmission of HIV [2] and from ever increasing knowledge of the details of the HIV transmission event [3].

Most recently, retrospective [4, 5] and observational [6–8] studies of discordant couples have reported greatly reduced transmission of HIV when an HIV-infected patient is receiving antiretroviral therapy (ART), at least over the short term. It has been estimated that for every 1-log decreases in HIV blood viral burden, a 2.5-fold reduced risk of HIV transmission is realized [4]. Inspired by these observations and deductive reasoning (eg, if ART drives down viral load, transmission risk should experience a de facto decrease), a Swiss HIV Advisory Committee formulated “The Swiss Statement,” which

indicated that, for treated patients in whom blood viral load was suppressed for 6 months, unprotected sex with an informed partner was acceptable [9].

In the current issue of *Clinical Infectious Diseases* [10], Swiss investigators surveyed 7309 patients with HIV infection from 2007 through 2009, most of whom (>80%) were successfully using ART. A substantial number of infected patients reported unprotected sex with their partners, and these behavioral decisions appear to have been influenced by knowledge of the blood viral load and the “Swiss statement” itself.

This could be considered an expected outcome of the “Swiss statement” for patients living in Switzerland [9], and perhaps putting condoms aside under some circumstances is a reasonable gamble. The overall risk of transmission of HIV is generally low during long-term HIV infection [11], and it is logical that ART should further reduce this risk [12].

But we have every reason to pause and reflect. The protection provided from ART is not absolute and is not absolutely predictable. In a study involving discordant couples in Africa, Sullivan et al [7] reported that 4 (2.3%) of 175 transmission events among a group of 2993 discordant couples occurred when the index patient was receiving therapy. In a very recent evaluation of discordant couples in Henan, China, 84 HIV transmission

events were noted among a group of 1927 couples who were followed-up from 2006 through 2008, and these transmission events were equally distributed among patients who were receiving and those who were not receiving ART [13]. Although it is very likely that the ART combinations and usage in the latter Chinese study were less than optimal (perhaps increasing the risk of an HIV transmission event), these are important real-world results [14].

Current ART regimens that suppress blood viral burden do not reliably suppress HIV replication in the male [15] or female genital tract [16], regardless of good penetration of most antiviral agents into these compartments (reviewed in [12]). In a very recent study, Cu-Uvin et al [16] reported that more than one-half of women who were receiving ART and had an undetectable level of HIV in blood had either intermittent or persistent recovery of HIV RNA in the genital tract, often at high –copy number. Although it is not known whether the viral copies detected in this and other studies represent “infectious units,” they surely represent a cause for concern.

Transmitted drug resistance (TDR) must also be taken into consideration. Although TDR has decreased in many countries as therapy has improved, it is still found in a substantial number of people with newly diagnosed HIV infection [17]. Such resistance must reflect acquisition of

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HIV from a partner who had stopped their therapy, or was using therapy imperfectly.

The Swiss Statement is not trivial. It helped to inspire widespread belief that treatment is prevention and to promote the now very popular “test and treat” movement, and no fewer than 5 “test and treat” population-based trials are in preparation [18]. In the current study [10], the authors note that the Swiss Statement appears to have inspired reduced use of condoms in at least some treated patients, who must now feel confident that the risk to their sexual partner is negligible. Yet critical and central questions remain unanswered: what is the actual risk of a transmission event within a discordant couple over time? Are the risks the same for unprotected vaginal and anal intercourse? Do all ART combinations confer the same protective benefit? how forgiving are the regimens in case of missed dosages?

Health care providers have no choice but to counsel patients and couples with the best available evidence. For vertical transmission of HIV, investigators have painstakingly defined the degree of protection afforded by ART offered to the mother and the baby and have worked hard to perfect this approach [2]. We can only hope that similar data will surface to direct the use of ART for prevention at both the clinical and population level. The actual benefits of “treatment as preven-

tion” may delight or disappoint us, but they certainly need to be determined, and soon.

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